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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/699,818	10/30/2000	Brian L. Ganz		7165

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EXAMINER	
GORDON, BRIAN R	
ART UNIT	PAPER NUMBER
1743	

DATE MAILED: 02/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

rnk-5

Office Action Summary	Application No.	Applicant(s)	
	09/699,818	GANZ ET AL.	
	Examiner	Art Unit	
	Brian R. Gordon	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6-33 and 37* is/are rejected.

7)☒ Claim(s) *3-5 and 34-36* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 January 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Arguments

1. Applicant's arguments filed January 13, 2002 with respect to claims 1-37 have been considered but are moot in view of the new ground(s) of rejection.

2. In light of applicant's arguments the objection to the specification as to failing to provide antecedent basis is hereby withdrawn.

Specification

3. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 103

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claims 1-2 and 32-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Salomaa et al. US 4,478,094 in view of Little US 6,024,925.

Salomaa et al. disclose an automatic liquid transfer system that includes a horizontally translatable table (microplate indexing device that also comprises a slide positioning station) and a vertically translatable set of pipettes (dispense head). The table accommodates a titer tray having a multiplicity of receptacles to be filled (slide positioning station), or holding liquid samples to be diluted, and a rack housing plural rows of disposable tips. During each cycle in a serial dilution process, a fresh set of

tips are picked up by the pipettes and used to transfer liquid in a sterile manner from a sample (solution removal area) or diluent source to a row of wells in the titer tray, or from one row to a succeeding row of wells where it is mixed with diluent.

Referring to FIGS. 1 and 2, an automatic serial dilution machine suitable for carrying out the method of the present invention includes two main movable parts, a horizontally translatable table 10 and a vertically translatable head assembly 12. As best illustrated in FIG. 2, the table 10 is mounted for horizontal translation on hardened guide rods 14 by means of slide bearings 16. Translation of the table is provided by a stepper motor 18 (actuator) through a pinion 20 connected to the motor and a rack 22 mounted on the underside of the table. Similarly, the head 12 is mounted for vertical translation on guide rods 24 by means of slide bearings 26. Translation of the head assembly is provided by a stepper motor 28 through a pinion 30 and a rack 32.

The head assembly 12 supports a pipette and plunger assembly 34. This assembly includes a series of pipettes 36 that are arranged in a row transverse to the axis of translation of the table 10.

The operation of each of the stepper motors 18, 28 and 46, and the solenoids 68 is controlled by a suitable microprocessor 70 (programmable computer). Basically, the microprocessor 70 functions as a pulse generator to control the sequence of operations of each of these elements, and thus the interrelated movements of the table 10, the head assembly 12, the plunger assembly 34 and the tip ejector plate 64 to effect serial dilution of a sample in the tray 54 at the forward work station 50.

FIGS. 12 to 14 illustrate an alternative embodiment of the moveable table arrangement of the present invention. This embodiment includes another microtiter tray 88 (solution removal area) between sample tray 54 and tip supply tray 56. Tray 88 may contain either a liquid supply of biological material or a reagent for initially filling the titer tray receptacles. While shown as a plurality of individual wells, tray 88 may be a common supply trough or pan. For example the initial charge of sample material may be injected into a first row of receptacles in tray 54 and after replacement of tips 62 from tray 56, the remaining wells in 56 filled with diluent transferred from another portion of tray 88 or a separate supply of liquid from another tray.

Salomaa et al. does not disclose that the substrate is a slide or that the device further comprises a light source and a camera.

Little et al. discloses parallel dispensing tools that can deliver defined and controlled volumes of fluid to generate multi-element arrays of sample material on a substrate surface. The substrates surfaces can be flat (slides) or geometrically altered to include wells of receiving material. FIG. 1 depicts a system 10 that includes a data processor 12, a motion controller 14, a robotic arm assembly 16, a monitor element 18A, a central processing unit 18B, a microliter plate of source material 20, a stage housing 22, a robotic arm 24, a stage 26 (isolated base), a pressure controller 28, a conduit 30, a mounting assembly 32, a pin assembly 38 (dispense head), and substrate elements 34. The interior chamber can be connected to a pressure source that will control the pressure within the interior chamber to regulate the flow of fluid within the interior chamber of the pins. In the view shown by FIG. 1, it is also

illustrated that the robotic assembly 16 can include a moveable mount element 40 and a horizontal slide groove 42. The robotic arm 24 can optionally pivot about a pin 36 to increase the travel range of the arm 24 so that arm 24 can dispose the pin assembly 38 above the source plate 20. The data processor 12 depicted in FIG. 1 can be a conventional digital data processing system such as an IBM PC compatible computer system that is suitable for processing data and for executing program instructions that will provide information for controlling the movement and operation of the robotic assembly 16. It will be apparent to one skilled in the art that the data processor unit 12 can be any type of system suitable for processing a program of instructions signals that will operate the robotic assembly 16. Optionally the data processor 12 can be a micro-controlled assembly that is integrated into the robotic housing 16. In further alternative embodiments, the system 10 need not be programmable and can be a single board computer having a firmware memory for storing instructions for operating the robotic assembly 16. In the embodiment depicted in FIG. 1, there is a controller 14 that electronically couples between the data processor 12 and the robotic assembly 16. The depicted controller 14 is a motion controller that drives the motor elements of the robotic assembly 16 for positioning the robotic arm 24 at a selected location. Additionally, the controller 14 can provide instructions to the robotic assembly 16 to direct the pressure controller 28 to control the volume of fluid ejected from the individual pin elements of the depicted pin assembly 38. The depicted robotic assembly 16 is a gantry system that includes an XY table for moving the robotic arm about an XY plane, and further includes a Z axis actuator (linear actuators) for moving

the robotic arm orthogonally to that XY plane.

FIG. 6A is a piezo electric transducer element which forms around the parameter of the capillary 112 and can transform an electrical pulse received from the pulse generator within a robotic assembly 16 to cause fluid to eject from the orifice 118 of the capillary 112.

After depositing the sample arrays onto the surface of the substrate, the arrays can be analyzed using any of a variety of means (e.g., spectrometric techniques, such as UV/IVIS, IR, fluorescence, chemiluminescence, NMR spectroscopy or mass spectrometry).

The matrix drops were observed by employing visualization via a CCD camera (column 16, lines 56-65).

It is also revealed that a windows based control software maybe employed as well as a strobe light is used to illuminate the tip of the dispenser in order for a camera to be employed to check the integrity and cleanliness of the tip.

Although Little does not mention that the substrate is a slide, it would have been obvious to one of the ordinary skill in the art to recognize that the flat substrate could be a slide. Furthermore it would have been also obvious to ordinary skill in the art modify the device of Salomaa to include the flat surface (slide) of Little to which sample arrays are dispensed to for identifying the presence of biomolecules (such as DNA) and their characteristics. It would have also been obvious to employ the use of the camera and strobe light of Little to check the cleanliness of the dispense head.

6. Claims 6-15, 17-19, 21-24, 26-27, 29, and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Salomaa in view of Little as applied to claims 1-2 and 32-33 above, and further in view of Palcic et al. US 6,026,174.

Although Salomaa in view of Little recites that a CCD Camera may be employed for visualization, it is not specifically recited that the camera supplies image data to a computer for analysis.

However, Palcic et al. US 6,026,174 discloses a system and method for automatically detecting diagnostic cells and cells having malignancy-associated changes (MAC).

The MAC detection system according to the present invention is shown in FIG. 1. The system 10 includes a digital microscope 12 that is controlled by and interfaced with a computer system 30. The microscope 12 preferably has a digital CCD camera 14 employing a scientific CCD having square pixels of approximately 0.3 mm by 0.3 mm size. The scientific CCD has a 100% fill factor and at least a 256 gray level resolution. The CCD camera is preferably mounted in the primary image plane of a planar objective lens 22 of the microscope 12. A stable light source 18, preferably with feedback control, illuminates the cell sample while an image of the slide is being captured by the CCD camera. The lens 22 placed between the sample 16 and the CCD camera 14 is preferably a 2x/0.75 objective that provides a depth of field in the range of 1-2 mm that yields a distortion-free image.

The images produced by the CCD camera are received by an image processing board 32 that serves as the interface between the digital camera 14 and

the computer system 30. The digital images are stored in the image processing board and manipulated to facilitate the detection of MACs. The image processing board creates a set of analog video signals from the digital image and feeds the video signals to an image monitor 36 in order to display an image of the objects viewed by the microscope.

An image of a frame from the slide is captured by the CCD camera and is transferred into the image processor. In this process, the CCD sensor within the camera cleared and a shutter of the camera is opened for a fixed period that is dependent on the intensity of the light source 18. After the image is optimized according to the steps described below, the stage then moves to a new position on the slide such that another image of the new frame can be captured by the camera and transferred into the computer memory. Because the cell sample on the slide occupies a much greater area than the area viewed by the microscope, a number of slide images are used to determine whether the sample is MAC-positive or negative. The position of each captured image on the slide is recorded in the computer system so that the objects of interest in the image can be found on the slide if desired.

Once an image from the slide is captured by the CCD camera and stored in the image processing board, the computer system determines whether the image produced by the CCD camera is devoid of objects. This is performed by scanning the digital image for dark pixels. If the number of dark pixels, i.e., those pixels having an intensity of the background intensity minus a predetermined offset value, is fewer than a predetermined minimum, the computer system assumes that the image is blank and

the microscope stage is moved to a new position at step 60 and a new image is captured at step 54.

It would have been obvious to one of ordinary skill in the art to modify the modified the modified device of Salomaa to allow for subsequent analysis of the deposited sample arrays in order to determine the presence of biological organisms and their characteristics. It would have also been obvious to use the camera of Little as employed by the method of Palcic and using the CCD camera present as an additional form or means of analysis (additional to e.g., spectrometric techniques, such as UV/IVIS, IR, fluorescence, chemiluminescence, NMR spectroscopy or mass spectrometry) for the samples deposited on the substrate.

As to claims 7-15 and 19, the examiner hereby submits that the claims are not structural limitations of the device but are moreso directed to the capability of the device and the data transmitted from the camera to the computer. The modified device of Salomaa is capable of performing in the manner recited in those claims.

As to claim 24, it would have also been obvious to provide the array on a vibration isolated base when one is attempting to dispense a precise volume of fluid when required.

7. Claims 16, 20, and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Salomaa in view of Little and Palcic as applied to claims 6-15, 17-19, 21-24, 26-27, 29, and 37 above, and further in view of and further in view of Ridgeway et al. US 5,879,628.

Salomaa in view of Little and Palcic does not disclose that a 2D bar code is used for identification of information.

Ridgeway discloses a device for handling samples in which a CPU maybe employed to control all operations. A bar code is also provided for containing information that is related to the reagents. The information can also be entered by way of a touch screen in conjunction with the keyboard. The device also employs the use of a rinsing station for flushing the inside and outside of the needle of the syringe system.

It would have been obvious to one of the ordinary skill to modify the modified device of Salomaa by employing the teachings of Ridgeway to include a washing station to allow for the reduction of cross-contamination and a bar code to store the related about the assay slide. As to the vacuum manifold, it would have been obvious to use a vacuum manifold as the pressure source for aspirating and dispensing the reagents for the array.

8. Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Salomaa et al. in view of Little and Palcic et al. as applied to claim claims 6-15, 17-19, 21-24, 26-27, 29, and 37 above, and further in view of Overbeck.

Salomaa et al. in view of Little and Palcic et al. does not disclose the use of quill type dispensers.

Overbeck discloses a fluid deposit assembly in which piezo and quill type dispensers are used to jet small volumes of fluid to a substrate.

It would have been obvious to one of the ordinary skill in the art at the time of the invention to modify the modified device of Little by employing the teachings of Overbeck

for quill and piezo dispensers are capable of depositing very small volumes of fluid as well as the employment of quill tips allows one to suck up a desired amount of fluid (column 2 lines 8-18).

Allowable Subject Matter

9. Claims 3-5 and 34-36 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

10. The following is an examiner's statement of reasons for allowance: the prior art does not teach or fairly suggest a microarray device that comprises an indexing device that comprises an input stacking chamber, an output stacking chamber, a walking bean indexer disposed between the input and output stacking chambers, and a lid lifter.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Lung et al., Hewett et al., Lancaster, Tseung et al., Meltzer, and Nakashima et al. disclose pipetting devices.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian R. Gordon whose telephone number is (703) 305-0399. The examiner can normally be reached on M-F, with 2nd and 4th F off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on 703-308-4037. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9310 for regular communications and (703) 872-9311 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.

brg
February 24, 2003

Jill Warden
Supervisory Patent Examiner
Technology Center 1700